Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptacmbl6447

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS 3	AUG 18	COMPENDEX indexing changed for the Corporate Source (CS) field
NEWS 4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS 5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS 6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS 7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS 8	OCT 21	Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS 9	OCT 21	Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS 10	NOV 23	Addition of SCAN format to selected STN databases
NEWS 11	NOV 23	Annual Reload of IFI Databases
NEWS 12	DEC 01	FRFULL Content and Search Enhancements
NEWS 13	DEC 01	DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets
NEWS 14	DEC 02	Derwent World Patent Index: Japanese FI-TERM thesaurus added
NEWS 15	DEC 02	PCTGEN enhanced with patent family and legal status display data from INPADOCDB
NEWS 16	DEC 02	USGENE: Enhanced coverage of bibliographic and sequence information

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

```
FILE 'HOME' ENTERED AT 12:24:00 ON 11 DEC 2009

=> file medline biosis caplus embase
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    0.22       0.22

FILE 'MEDLINE' ENTERED AT 12:24:23 ON 11 DEC 2009

FILE 'BIOSIS' ENTERED AT 12:24:23 ON 11 DEC 2009
Copyright (c) 2009 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 12:24:23 ON 11 DEC 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 12:24:23 ON 11 DEC 2009
Copyright (c) 2009 Elsevier B.V. All rights reserved.

=> s (fsh or follicle(w)stimulating(w)hormone)
L1      142743 (FSH OR FOLLICLE(W) STIMULATING(W) HORMONE)

=> s l1 and (alpha(w)subunit) and (lysine or arginine) and (mutein or mutation or
variant)
L2           15 L1 AND (ALPHA(W) SUBUNIT) AND (LYSINE OR ARGININE) AND (MUTEIN
                OR MUTATION OR VARIANT)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           14 DUP REM L2 (1 DUPLICATE REMOVED)

=> dis ibib abs l3 1-14

L3   ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2008:677125  CAPLUS
DOCUMENT NUMBER:          149:45404
TITLE:                    Suppression of Inhibin A Biological Activity by
                          Alterations in the Binding Site for Betaglycan
AUTHOR(S):                Makanji, Yogeshwar; Walton, Kelly L.; Wilce, Matthew
                          C.; Chan, Karen L.; Robertson, David M.; Harrison,
                          Craig A.
CORPORATE SOURCE:         Prince Henry's Institute of Medical Research, Clayton,
                          Victoria, 3168, Australia
SOURCE:                   Journal of Biological Chemistry (2008), 283(24),
                          16743-16751
                          CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:                American Society for Biochemistry and Molecular
                          Biology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Inhibins A and B neg. regulate the production and secretion of FSH
     from the anterior pituitary, control ovarian follicle development and
     steroidogenesis, and act as tumor suppressors in the gonads.  Inhibins
     regulate these reproductive events by forming high affinity complexes with
     betaglycan and activin or bone morphogenetic protein type II receptors.
     In this study, the binding site of inhibin A for betaglycan was
     characterized using inhibin A mutant proteins.  An epitope for high
     affinity betaglycan binding was detected spanning the outer convex surface
     of the inhibin α -subunit.  Homol. modeling
     indicates that key α -subunit residues (Tyr50,
```

Val108, Thr111, Ser112, Phe118, Lys119, and Tyr120) form a contiguous epitope in this region of the mol. Disruption of betaglycan binding by the simultaneous substitution of Thr111, Ser112, and Tyr120 to alanine yielded an inhibin A variant that was unable to suppress activin-induced FSH release by rat pituitary cells in culture. Together these results indicate that a high affinity interaction between betaglycan and residues Val108-Tyr120 of the inhibin α - subunit mediate inhibin A biol. activity.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 14 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2008290765 EMBASE

TITLE: Regulation of spermatogenesis in McCune-Albright syndrome: Lessons from a 15-year follow-up.

AUTHOR: De Luca, Filippo (correspondence); Wasniewska, Malgorzata; Arrigo, Teresa; Messina, Maria Francesca; Valenzise, Mariella

CORPORATE SOURCE: Department of Pediatrics, University of Messina, 01924 Messina, Italy. wasniewska@yahoo.it

AUTHOR: Mitchell, Valerie

CORPORATE SOURCE: Laboratory of Spermiology and Histology, CHRU, Faculty of Medicine, 59037 Lille, France.

AUTHOR: de Sanctis, Luisa

CORPORATE SOURCE: Department of Pediatrics, University of Turin, 10126 Turin, Italy.

AUTHOR: Lahlou, Najiba

CORPORATE SOURCE: Laboratory for Hormone Biology, CHU Cochin - Saint Vincent de Paul, 75014 Paris, France.

AUTHOR: De Luca, Filippo (correspondence)

CORPORATE SOURCE: Dipartimento di Scienze Pediatriche Mediche e Chirurgiche, Policlinico Universitario di Messina, Via Consolare Valeria, 98123 Messina, Italy. wasniewska@yahoo.it

SOURCE: European Journal of Endocrinology, (Jun 2008) Vol. 158, No. 6, pp. 921-927.
Refs: 28
ISSN: 0804-4643 CODEN: EJOEEP

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 028 Urology and Nephrology
003 Endocrinology
033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 27 Jun 2008
Last Updated on STN: 27 Jun 2008

AB Context: McCune-Albright syndrome (MAS) is a disorder caused by a post-zygotic gain-of-function mutation in the gene encoding the Gs-α protein. Sexual precocity, common in girls, has been reported in only 15% of boys, and little is known on the long-term evolution of MAS in males. Objective: In a boy with MAS, we studied spermatogenesis, testis histology, and immunohistochemistry with the aim to shed light on seminiferous tubule activity. Design: A boy who presented at the age of 2.9 years with sexual precocity, monolateral macroorchidism, increased testosterone levels, and suppressed gonadotropins was followed up until the age of 18. Results: Throughout follow-up testicular asymmetry

persisted and gonadotropin and testosterone pattern did not change. At the age of 18, inhibin B was undetectable while a-immunoreactive inhibin was within normal range. Anti-Mullerian hormone level was slightly subnonnal. Sperm cells were 3 900 000 per ejaculate. Histology of both testes showed spermatogonia, spermatocytes, and, in some tubes, matured spermatozoa. Sertoli cells were markedly stained with anti-inhibin . alpha.-subunit antibody in both the testes. There was no immunostaining of Sertoli, Leydig, or germ cells with anti-βA or anti-βB antibody. MAS R201H mutation was identified in both the testes. Conclusion: The 15-year follow-up in this boy with MAS demonstrated that autonomous testicular activation and gonadotropin suppression persisted over time. This provides an interesting model of active spermatogenesis despite long-term FSH suppression. It also suggests that FSH is needed for the full expression of the inhibin βB-subunit gene, an expression previously reported in the germ and Leydig cells of normal adult subjects. .COPYRGT. 2008 Society of the European Journal of Endocrinology.

L3 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:817105 CAPLUS
DOCUMENT NUMBER: 147:182868
TITLE: Use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances
INVENTOR(S): Mendrick, Donna L.; Johnson, Kory R.; Daniels, Kellye K.; Porter, Mark W.
PATENT ASSIGNEE(S): Gene Logic, Inc., USA
SOURCE: PCT Int. Appl., 203pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007084187	A2	20070726	WO 2006-US33712	20060828
WO 2007084187	A3	20090827		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
US 20090202995	A1	20090813	US 2008-64933	20080930
PRIORITY APPLN. INFO.:			US 2005-711444P P	20050826
			WO 2006-US33712 W	20060828

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention includes methods of predicting cardiotoxicity of test agents and methods of generating cardiotoxicity prediction models using algorithms for analyzing quant. gene expression information. The invention also includes microarrays, computer systems comprising the toxicity prediction models, as well as methods of using the computer systems by remote users for determining the toxicity of test agents.

L3 ANSWER 4 OF 14 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 2006575622 EMBASE

TITLE: Role of the intracellular domains of the human FSH receptor in GαS protein coupling and receptor expression.

AUTHOR: Ulloa-Aguirre, Alfredo (correspondence); Uribe, Aida; Zarinan, Teresa; Perez-Solis, Marco A.

CORPORATE SOURCE: Research Unit in Reproductive Medicine, Hospital de Ginecobstetricia Luis Castelazo Ayala, Instituto Mexicano del Seguro Social, Apartado Postal 99-065, Mexico 10101 D.F., Mexico. aulloaa@servidor.unam.mx

AUTHOR: Bustos-Jaimes, Ismael

CORPORATE SOURCE: Department of Biochemistry, Faculty of Medicine, Universidad Nacional Autonoma de Mexico, Mexico D.F., Mexico.

AUTHOR: Dias, James A.

CORPORATE SOURCE: Wadsworth Center, David Axelrod Institute for Public Health, Albany, NY, United States.

SOURCE: Molecular and Cellular Endocrinology, (2 Jan 2007) Vol. 260-262, pp. 153-162.
Refs: 84
ISSN: 0303-7207 CODEN: MCEND6

PUBLISHER IDENT.: S 0303-7207(06)00442-4

COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical and Experimental Biochemistry
003 Endocrinology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 12 Dec 2006
Last Updated on STN: 12 Dec 2006

AB The human (h) follicle-stimulating hormone receptor (FSHR) belongs to the superfamily of G protein-coupled receptors (GPCRs). This receptor consists of 695 amino acid residues and is preferentially coupled to the Gs protein. This receptor is highly conserved among species (overall homology, 85%), with a 25-69% homology drop when compared to the human LH and TSH receptors. Although studies in prototypical rhodopsin/β-adrenergic receptors suggest that multiple domains in the intracellular loops (iL) and the carboxyl-terminus (Ctail) of these receptors contribute to G protein coupling and receptor expression, there is a paucity of structure/function data on the role of these domains in FSHR function. Employing point mutations we have found that several residues present in the iL2 of the hFSHR are important for both coupling the receptor to the Gs protein and maintaining the receptor molecule in an inactive conformation. In fact, HEK-293 cells expressing several hFSHR mutants with substitutions at R450 (central to the highly conserved ERW triplet motif) and T453 (a potential target for phosphorylation) failed to mediate ligand-provoked Gs protein activation but not agonist binding, whereas substitutions at the hydrophobic L460 (a conserved residue present in all glycoprotein hormone receptors) conferred elevated basal cAMP to the transfected cells. Thus, this particular loop apparently acts as a conformational switch for allowing the receptor to adopt an active conformation upon agonist stimulation. Residues in both ends of the iL3 are important for signal transduction in a number of GPCRs, including the FSHR. We have recently explored the importance of the reversed BBXXB motif (BXXBB; where B represents a basic residue and X a non-basic residue) present in the juxtamembrane region of the hFSHR iL3. A hFSHR mutant with all basic amino acids present in the iL3 BXXBB motif replaced by alanine failed to bind agonist and activate effector, and was expressed as an immature ≤62 kDa form of the receptor. Individual substitutions of basic residues resulted in mutants that bound agonist normally but failed to activate effector when replaced at R552 or R556.

Triple mutations in the same motif located in the NH2-end of the Ctail resulted in a complete inability of the receptor to bind agonist and activate effector, whereas individual substitutions resulted in decreased or virtually abolished agonist binding and cAMP accumulation, with both functions correlating with the detected levels of mature (80 kDa) forms of the receptor. Thus, the BXXBB motif at the iL3 of the FSHR is essential for coupling the activated receptor to the Gs protein, whereas the same motif in the Ctail is apparently more important for membrane expression. The role of cysteine residues present in the Ctail of the FSHR is an enigma since there are no conserved cysteines amongst LHR, FSHR and TSHR. C629 and C655 are conserved in the gonadotropin receptors but not in the TSHR. Alanine replacement of C627 had no effect on hFSHR expression and function, whereas the same mutation at C629 altered membrane expression and signal transduction. Serine or threonine substitutions of C655 did not modify any of the parameters analyzed. In the hFSHR, C629 may be a target for palmitoylation, and apparently it is the only cysteine residue in the Ctail domain that might play an important role in receptor function. .COPYRGT. 2006 Elsevier Ireland Ltd. All rights reserved.

L3 ANSWER 5 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2004518428 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15304512
TITLE: Only a portion of the small seatbelt loop in human choriogonadotropin appears capable of contacting the lutropin receptor.
AUTHOR: Bernard Michael P; Lin Win; Cao Donghui; Myers Rebecca V; Xing Yongna; Moyle William R
CORPORATE SOURCE: Department of OB-GYN, Robert Wood Johnson (Rutgers) Medical School, Piscataway, New Jersey 08854, USA.
CONTRACT NUMBER: HD14907 (United States NICHD NIH HHS)
HD28547 (United States NICHD NIH HHS)
SOURCE: The Journal of biological chemistry, (2004 Oct 22) Vol. 279, No. 43, pp. 44438-41. Electronic Publication: 2004-08-10.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 19 Oct 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 14 Dec 2004

AB Twenty residues of the human choriogonadotropin (hCG) beta-subunit that are wrapped around alpha-subunit loop 2 like a "seatbelt" stabilize the heterodimer and enable the hormone to distinguish lutropin (LHR), follitropin, and thyrotropin receptors. The N-terminal portion of the seatbelt contains a small disulfide-stabilized loop needed for heterodimer assembly and is thought to mediate hCG-LHR interactions. To test the latter notion, we compared the LHR binding and signal transduction activities of hCG analogs in which the alpha-subunit C terminus (alphaCT) was cross-linked to residues in the small seatbelt loop. Analogs having an intersubunit disulfide between a cysteine in place of alphaCT residue alphaSer-92 and cysteines substituted for loop residues betaArg-94, betaArg-95, or betaSer-96 had high activities in LHR binding and signaling assays despite the fact that both portions of the hormone are thought to be essential for hCG activity. Use of a larger probe blocked hormone activity when the alphaCT was cross-linked to cysteines in place of residues betaArg-95 and betaAsp-99, but not to cysteines in place of residues betaArg-94, betaSer-96, or betaThr-97. This suggested that the side chains of residues betaArg-95

and betaAsp-99, which face in the same outward direction from the heterodimer, are nearer than the others to the LHR interface. The finding that residue 95 can be cross-linked to small alphaCT probes without eliminating hormone activity indicates its side chain does not participate in essential LHR contacts. We suggest that contacts between the small seatbelt loop and the LHR, if any, involve its backbone atoms and possibly the side chain of residue betaAsp-99.

L3 ANSWER 6 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003429279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12970262
TITLE: Growth hormone deficiency in pseudohypoparathyroidism type 1a: another manifestation of multihormone resistance.
AUTHOR: Germain-Lee Emily L; Groman Joshua; Crane Janet L; Jan de Beur Suzanne M; Levine Michael A
CORPORATE SOURCE: Department of Pediatrics, Division of Endocrinology and the Ilyssa Center for Molecular Endocrinology, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA.. egermain@jhmi.edu
CONTRACT NUMBER: M01 RR00052 (United States NCRR NIH HHS)
PA-99106 R01 DK56178 (United States NIDDK NIH HHS)
R01 DK56178 (United States NIDDK NIH HHS)
SOURCE: The Journal of clinical endocrinology and metabolism, (2003 Sep) Vol. 88, No. 9, pp. 4059-69.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 13 Sep 2003
Last Updated on STN: 11 Oct 2003
Entered Medline: 10 Oct 2003

AB Albright hereditary osteodystrophy (AHO) is a genetic disorder caused by heterozygous inactivating mutations in GNAS1, the gene encoding the alpha-chain of G(s), and is associated with short stature, obesity, brachydactyly, and sc ossifications. AHO patients with GNAS1 mutations on maternally inherited alleles also manifest resistance to multiple hormones (e.g. PTH, TSH, LH, FSH), a variant termed pseudohypoparathyroidism (PHP) type 1a, due to paternal imprinting of G alpha(s) transcripts in specific tissues. Recent evidence has shown that G alpha(s) transcripts are also imprinted in the pituitary somatotrophs that secrete GH. Because this imprinting could influence GHRH-dependent stimulation of somatotrophs, we hypothesized that maternally inherited GNAS1 mutations would impair GH secretion. We studied GH status in 13 subjects with PHP type 1a. GH responses to arginine/L-dopa and arginine/GHRH were deficient in nine subjects, all of whom were obese and had low serum concentrations of IGF-I. By contrast, none of the four GH-sufficient subjects were obese, and all had normal IGF-I levels. Our data indicate that GH deficiency is common (69%) in PHP type 1a and may contribute to the obesity and short stature typical of AHO. We propose that GH status be evaluated in all patients with PHP type 1a.

L3 ANSWER 7 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003058634 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12568849
TITLE: Analysis of the Cys82Arg mutation in follicle-stimulating hormone beta (FSHbeta) using a novel FSH expression

vector.
AUTHOR: Clark Andrew D; Layman Lawrence C
CORPORATE SOURCE: Section of Reproductive Endocrinology, Infertility and Genetics, Department of Obstetrics and Gynecology, Medical College of Georgia, Augusta, Georgia 30912, USA.
CONTRACT NUMBER: HD 33004 (United States NICHD NIH HHS)
SOURCE: Fertility and sterility, (2003 Feb) Vol. 79, No. 2, pp. 379-85.
Journal code: 0372772. ISSN: 0015-0282.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 6 Feb 2003
Last Updated on STN: 4 Apr 2003
Entered Medline: 3 Apr 2003

AB OBJECTIVE: To determine the effect of the Cys82Arg FSHbeta mutation from a patient with isolated FSH deficiency upon follicle-stimulating hormone (FSH) levels in vitro. DESIGN: In vitro analysis of the Cys82Arg mutation and comparison with the phenotype. SETTING: Tertiary medical center setting. PATIENT(S): DNA sequence of the FSHbeta gene and clinical description from a patient with isolated FSH deficiency. INTERVENTION(S): Construction of a new vector containing the cDNAs for the alpha-subunit and beta-subunit of FSH (palphaFSHbeta) followed by mutagenesis and transfection into Chinese hamster ovary cells. MAIN OUTCOME MEASURE(S): Immunoreactive and bioactive FSH levels from the CHO cellular media. RESULT(S): Although expression of both subunits was present, both immunoreactive and bioactive FSH levels were unmeasurable from cellular media containing the mutation versus wild type. CONCLUSION(S): The Cys82Arg mutation in a male with normal puberty and azoospermia results in profound deficiency of FSH in vitro, thereby confirming the molecular basis of hypogonadism in this patient and documenting the importance of the Cys residue at position 82 of the FSHbeta subunit.

L3 ANSWER 8 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2002441483 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12199347
TITLE: Premature thelarche and granulosa cell tumors: a search for FSH receptor and G5alpha activating mutations.
AUTHOR: Hannon Tamara S; King Denise Walker; Brinkman Abigail D; Steinmetz Rosemary; Davis Mary M; Eugster Erica A; Pescovitz Ora H
CORPORATE SOURCE: Department of Pediatrics, James Whitcomb Riley Hospital for Children, Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis 46202, USA.. tshannon@iupui.edu
SOURCE: Journal of pediatric endocrinology & metabolism : JPEM, (2002) Vol. 15 Suppl 3, pp. 891-5.
Journal code: 9508900. ISSN: 0334-018X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 30 Aug 2002
Last Updated on STN: 19 Mar 2003
Entered Medline: 18 Mar 2003

AB Activating mutations of the Gsalpha gene are responsible for McCune-Albright syndrome and have also been identified in sporadic tumors of the pituitary and thyroid. When associated with malignancy, activating Gsalpha mutations are known as gsp-oncogenes. We hypothesized that similar activating mutations might also account for some cases of premature thelarche and/ or granulosa cell tumors. Polymerase chain reaction and DNA sequencing was used to screen for activating mutations of Gsalpha genes in children with premature thelarche and in pathologic specimens from juvenile and adult granulosa cell tumors. Because these disorders involve over-activity of the FSH -signaling pathway, we also screened for activating mutations of the FSH receptor. No mutations were detected in either the Gsalpha or the FSHR fragment studied. Previously reported polymorphisms (Ser680Asn and Ala307Thr) of the FSHR were detected in 25/27 tumor samples and 9/9 premature thelarche samples. We conclude that activating mutations in previously identified mutation 'hot-spots' in the Gsalpha and FSH receptor genes are probably not a major cause of premature thelarche or granulosa cell tumors. In contrast, polymorphisms of the FSH receptor are common.

L3 ANSWER 9 OF 14 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:441859 BIOSIS
DOCUMENT NUMBER: PREV200100441859
TITLE: Partial restoration of lutropin activity by an intersubunit disulfide bond: Implications for structure/function studies.
AUTHOR(S): Einstein, Monica; Lin, Win; Macdonald, Gordon J.; Moyle, William R. [Reprint author]
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Robert Wood Johnson (Rutgers) Medical School, 675 Hoes Lane, Piscataway, NJ, 08854, USA
moyle@umdnj.edu
SOURCE: Experimental Biology and Medicine (Maywood), (June, 2001) Vol. 226, No. 6, pp. 581-590. print.
ISSN: 1535-3702.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 2001
Last Updated on STN: 22 Feb 2002

AB Gonadal function is controlled by lutropins and follitropins, heterodimeric cystine knot proteins that have nearly identical alpha-subunits. These heterodimeric proteins are stabilized by a portion of the hormone-specific beta-subunit termed the "seatbelt" that is wrapped around alpha-subunit loop 2 (alpha2). Here we show that replacing human chorionic gonadotropin (hCG) alpha2 residue Lys51 with cysteine or alanine nearly abolished its lutropin activity, an observation that implies that alphaLys51 has a key role in hormone activity. The activity of the heterodimer containing alphaK51C, but not that containing alphaK51A, was increased substantially when beta-subunit seatbelt residue betaAsp99 was converted to cysteine. As had been reported by others, heterodimers containing alphaK51C and betaD99C were crosslinked by a disulfide. The finding that an intersubunit disulfide restored some of the activity lost by replacing alphaLys51 suggests that this residue is not crucial for receptor binding or signaling and also that hCG and related hormones may be particularly sensitive to mutations that alter interactions between their subunits. We propose the unique structures of hCG and related family

members may permit some subunit movement in the heterodimer, making it difficult to deduce key residues involved in receptor contacts simply by correlating the activities of hormone analogs with their amino acid sequences.

L3 ANSWER 10 OF 14 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001131062 EMBASE
TITLE: β-Subunit 102-104 residues are crucial to confer FSH activity to equine LH/CG but are not sufficient to confer FSH activity to human CG.
AUTHOR: Chopineau, M. (correspondence); Martinat, N.; Galet, C.; Guillou, F.; Combarnous, Y.
CORPORATE SOURCE: Station de Physiol. Reprod. Comport., Inst. Natl. de la Rech. Agronomique, UMR 6073, 37380 Nouzilly, France. chopinea@tours.inra.fr
SOURCE: Journal of Endocrinology, (2001) Vol. 169, No. 1, pp. 55-63.
Refs: 28
ISSN: 0022-0795 CODEN: JOENAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Apr 2001
Last Updated on STN: 30 Apr 2001

AB Horse LH/CG (eLH/CG) and donkey LH/CG (dkLH/CG) are strictly LH-specific in their respective homologous species. However, both bind to the FSH receptors from non-equid species, whereas the zebra hormone (zbLH/CG) does not. The FSH/LH ratio of eLH/CG and of the αdkβe hybrid is about tenfold higher than that of dkLH/CG and of the αeβdk hybrid, showing that the βe subunit contains the structural features responsible for the high FSH activity of eLH/CG. Only six amino acid positions (51, 94, 95, 102, 103 and 106) are unique to the βe subunit when compared with the βdk and βzb subunits. The Gly-Pro and Val-Phe sequences in positions 102-103 of βdk and βe respectively were swapped by site-directed mutations and the mutated β-subunits cDNAs were cotransfected in COS cells with either αe or αdk subunit cDNA. Other mutations were also introduced in 102-103 dkLH/CG β-subunit: Ala-Ala, Gly-Ala or Ala-Pro. These mutations with Ala-Ala, Gly-Ala or Ala-Pro in the 102-103 βdkLH/CG subunit did not change the FSH/LH ratio of dkLH/CG but the heterodimers containing αe or αdk. Conversely, the Val102-Phe103 mutation in βe led to a dramatic drop in FSH/LH activity ratio of eLH/CG, to a level similar to that of dkLH/CG. Since all FSHs possess a Gly residue at position 104, we introduced the Gly102-Pro103-Arg104→Val102-Phe103-Gly104 mutation in βdk with the expectation that the increase in FSH activity observed with the Gly102-Pro103→Val102-Phe103 mutation could be potentiated. In fact, the additional Arg104→Gly104 mutation was found to abolish the increase in FSH activity observed with Gly102-Pro103→Val102-Phe103. Mutations Gly102-Pro103→Val102-Arg103 or Gly102-Pro103-Lys104→ Val102-Arg103-Gly104 were also introduced in human CGβ (hCGβ) to compare the impact of these amino acid changes in the well-studied gonadotrophin hCG. The βbCG mutants obtained, co-expressed either with the human or the horse .alpha .-subunit, did not display any FSH activity. In conclusion, the 102-104 sequence in eLH/CG β-subunits appears to be

of utmost importance for their binding to FSH receptors. However, these results obtained with equid β-subunits are not transposable to other gonadotrophins as similar mutations in hCGβ did not lead to any increase in FSH activity.

L3 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:340938 CAPLUS
DOCUMENT NUMBER: 125:26466
ORIGINAL REFERENCE NO.: 125:4999a,5002a
TITLE: Site-directed mutagenesis of amino acids 33-44 of the common α -subunit reveals different structural requirements for heterodimer expression among the glycoprotein hormones and suggests that cyclic adenosine 3',5'-monophosphate production and growth promotion are potentially dissociable functions of human thyrotropin
AUTHOR(S): Grossmann, Mathis; Szkudlinski, Mariusz W.; Dias, James A.; Xia, Haiying; Wong, Rosemary; Puett, David; Weintraub, Bruce D.
CORPORATE SOURCE: Natl. Inst. Diabetes Digestive Kidney Dis., Natl. Inst. Health, Bethesda, MD, 20892-1758, USA
SOURCE: Molecular Endocrinology (1996), 10(6), 769-779
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid residues 33-44 of the common α -subunit of the glycoprotein hormones have been implicated in heterodimerization as well as high affinity receptor binding of human (h) CG. In the present study, we compared the role of specific amino acids within this region for glycoprotein hormone heterodimer formation, using a transient transfection system to coexpress different mutant α -subunit constructs with the β-subunit of either hTSH, hCG, or hFSH. Our results identified a crucial role for αPro38 in the heterodimer expression of hTSH as well as hFSH, similar to what had been described for hCG. In contrast, αAla36, which had been critical for hCG, was not essential for hTSH heterodimer expression and less important for hFSH, whereas αPhe33 and αArg35 appeared uniquely important for hFSH. Furthermore, we assessed the role of these residues for bioactivity and receptor binding of hTSH. Mutation of the surface-exposed residues αArg42-Ser43-Lys44, which form part of a unique α-helical structure, to Ala42-A;a43-Ala44, decreased TSH receptor binding using porcine thyroid membranes as well as rat FRTL-5 cells. Residues αPhe33 and αArg35, in contrast, were not important for high affinity binding of hTSH. In the signal transduction of hTSH, αAla36 was necessary for efficient growth induction in FRTL-5 cells but not for cAMP production in either FRTL-5 cells or Chinese hamster ovary cells expressing the human TSH receptor (JP09). Similarly, residues αArg42-Ser43-Lys44 were more important for hTSH-mediated induction of cell growth than cAMP production Mutating αArg35 to Ala reduced cAMP induction but not receptor binding of hTSH. In summary, using site-directed mutagenesis, we identified a domain, residues 33-44 of the common α -subunit, important in heterodimer expression, receptor binding, and activation of hTSH. The comparison of the relative roles of specific amino acids within this region in hTSH with hCG and hFSH highlights previously unrecognized differences in the structural requirements for heterodimer expression among the members of the glycoprotein hormone family. Moreover, our findings revealed a novel role for residues α33-44 in triggering different postreceptor events, suggesting that cAMP production and growth promotion may, at least in part, be dissociable functions of hTSH.
OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS

RECORD (23 CITINGS)

L3 ANSWER 12 OF 14 MEDLINE on STN
ACCESSION NUMBER: 1995237161 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7536667
TITLE: Role of the Pro-Leu-Arg motif in glycosylation of human gonadotropin alpha-subunit.
AUTHOR: Furuhashi M; Suzuki S; Tomoda Y; Suganuma N
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Nagoya University School of Medicine, Japan.
SOURCE: Endocrinology, (1995 May) Vol. 136, No. 5, pp. 2270-5. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 5 Jun 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 23 May 1995

AB CG, LH, FSH, and TSH are a family of heterodimeric glycoprotein hormones that contain a common alpha-subunit, but differ in their hormone-specific beta-subunit. Processing of the N-linked oligosaccharide of the glycoprotein family is both tissue and dimer specific. LH, TSH, and free alpha synthesized in pituitary bear oligosaccharide terminating with sulfate (SO4) and N-acetylgalactosamine (GalNAc), whereas the termination of oligosaccharide in CG synthesized in placenta and FSH is sialic acid and galactose (Gal). Using site-directed mutagenesis and gene transfer, we studied the role of the Pro-Leu-Arg motif, which has been shown to be a recognition marker of glycoprotein hormone-specific GalNAc transferase, in sulfation of N-linked oligosaccharide in alpha-subunit. The wild-type or mutated alpha gene was transfected into GH3 cells. Our data revealed that substitution of the Pro-Leu-Arg motif by Ala-Leu-Ala did not affect the sulfation of N-linked oligosaccharide, but generated the attachment of O-linked oligosaccharide. alpha-Subunit containing either of the two N-linked glycosylations is also sulfated. We conclude that in GH3 cells, the Pro-Leu-Arg motif plays no role in the sulfation of oligosaccharide in alpha-subunit, and both N-glycosylations are terminated with SO4.

L3 ANSWER 13 OF 14 EMBASE
ACCESSION NUMBER: 1993320668 EMBASE
TITLE: Site-directed alanine mutagenesis of Phe33, Arg35, and Arg42- Ser43-Lys44 in the human gonadotropin .alpha .-subunit.
AUTHOR: Liu, C.; Roth, K.E.; Shepard, B.A.L.; Shaffer, J.B.; Dias, J.A. (correspondence)
CORPORATE SOURCE: Wadsworth Center for Lab./Research, New York State Department of Health, P. O. Box 509, Albany, NY 12201-0509, United States.
SOURCE: Journal of Biological Chemistry, (1993) Vol. 268, No. 29, pp. 21613-21617.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Dec 1993

Last Updated on STN: 5 Dec 1993

AB Residues Phe33 and Arg35, individually, and a composite mutation of residues Arg42, Ser43, and Lys44 were changed to alanine in the human glycoprotein hormone common α -subunit using site-directed mutagenesis. These specific residues are highly conserved across species and have by chemical modification and synthetic peptide approaches been implicated in the binding of human chorionic gonadotropin (hCG) to leutinizing hormone (LH) receptor. In the present study we tested the hypothesis that specific α -subunit amino acid residues which stabilize the hormone receptor interaction for hCG have the same function in human follicle-stimulating hormone (hFSH). Wild type or mutant α - subunit cDNAs were coexpressed with wild type hFSH or hCGβ cDNA in sialylation defective Chinese hamster ovary cells. Recombinant hormones were tested in a radioligand receptor competition assay, using rat testis membranes as a source of FSH and LH receptors. Mutant hFSH heterodimers F33A- FSH, R35A-FSH, Arg42-Ser43-Lys44/Ala42-Ala43-Ala44-FSH all displaced 125I-hFSH in a similar fashion, indicating that these residues are not important for binding of hFSH to the rat FSH receptor. On the other hand, F33A-CG evidenced a 5-fold decrease in binding, while R35A-CG had over a 100-fold decrease in binding to the rat LH receptor when compared to the wild type recombinant hCG. These data demonstrate that a receptor-binding site on the common α -subunit which is very important for hCG binding to LH receptor is not important for the binding of hFSH to FSH receptor. Our interpretation of these findings is that there are fundamental structural differences in the receptor interface contacts of the common α -subunit, which stabilize receptor binding among members of the glycoprotein hormone family.

L3 ANSWER 14 OF 14 MEDLINE on STN

ACCESSION NUMBER:	1993380952 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 8396579
TITLE:	Activating mutations of the Gs alpha-gene in nonfunctioning pituitary tumors.
AUTHOR:	Tordjman K; Stern N; Ouaknine G; Yossiphov Y; Razon N; Nordenskjold M; Friedman E
CORPORATE SOURCE:	Institute of Endocrinology, Elias Sourasky Tel-Aviv Medical Center, Tel-Aviv University Sackler School of Medicine, Israel.
SOURCE:	The Journal of clinical endocrinology and metabolism, (1993 Sep) Vol. 77, No. 3, pp. 765-9. Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:	English
FILE SEGMENT:	Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:	199310
ENTRY DATE:	Entered STN: 29 Oct 1993 Last Updated on STN: 3 Mar 2000 Entered Medline: 14 Oct 1993

AB The majority of pituitary tumors are of monoclonal origin; however, the molecular basis for their formation is poorly understood. Somatic mutations in the alpha-subunit of the GTP-binding protein, Gs alpha (gsp oncogene) have been found in about one third of GH-secreting tumors. Mutations in another alpha-subunit of a GTP-binding protein, Gi2 alpha (gip mutations) have been described in other endocrine tumors. In this study, we examined 21 nonfunctioning pituitary tumors and 4 macroprolactinomas for gsp mutations and 27 nonfunctioning

tumors and 4 macroprolactinomas for gip mutations. Using the polymerase chain reaction and denaturing gradient gel electrophoresis, 2 nonfunctioning pituitary tumors displayed migration abnormalities when the Gs alpha-gene was analyzed. Sequence analysis of these abnormally migrating polymerase chain reaction products revealed two previously known gsp mutations: arginine at codon 201 altered to cysteine, and glutamine at codon 227 changed to leucine. No gip mutations could be demonstrated. These findings emphasize the monoclonal origin of nonfunctioning pituitary tumors and suggest that cAMP may play a role in tumorigenesis of nonfunctioning pituitary tumors.

```
=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

     (FILE 'HOME' ENTERED AT 12:24:00 ON 11 DEC 2009)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 12:24:23 ON 11 DEC 2009
L1       142743 SEA FILE=MFE SPE=ON  ABB=ON  PLU=ON  (FSH OR FOLLICLE(W)
                STIMULATING(W) HORMONE)
L2           15 SEA FILE=MFE SPE=ON  ABB=ON  PLU=ON  L1 AND (ALPHA(W) SUBUNIT)
                AND (LYSINE OR ARGININE) AND (MUTEIN OR MUTATION OR VARIANT)
L3           14 DUP REM L2 (1 DUPLICATE REMOVED)
                DIS IBIB ABS L3 1-14
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                59.76      59.98

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -2.46      -2.46

STN INTERNATIONAL LOGOFF AT 12:27:39 ON 11 DEC 2009
```